SM.

Notice of Allowability	Application No.	Applicant(s)	
	09/748,063	MCHALE ET AL.	
	Examiner	Art Unit	
	Richard Schnizer, Ph. D	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *12/22/03*.

2. ☒ The allowed claim(s) is/are *2,5-8 and 11-23*.

3. ☒ The drawings filed on *22 December 2003* are accepted by the Examiner.

4. ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☒ None of the:
      1. ☒ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: *PCT/GB00/02828 07/24/2000*
   UNITED KINGDOM 9917416.1 07/23/1999.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date 11/4/03
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Tom Kowalski on 3/12/04.

The application has been amended without prejudice as follows:

1. (cancelled)

2. (currently amended) The method according to claim [1] 8, wherein the sensitising comprises the step of applying an electric pulse to [a] the red blood cell.

3. (cancelled)

4. (cancelled)

5. (currently amended) The method according to claim [1] 8, in which the sensitisation of the red blood cell precedes the loading of the agent.

6. (currently amended) The method according to claim [1] 8, in which the loading of the agent precedes the sensitisation of the red blood cell.

7. (currently amended)The method according to claim [1] 8, in which the sensitisation of the red blood cell and the loading of the agent are simultaneous.

8. (currently amended) A method for selectively releasing an agent from a red blood cell comprising the steps of:

(a) loading [a] the red blood cell with [an] the agent *in vitro* or *ex-vivo*;

(b) sensitising *in vitro* or *ex-vivo* the red blood cell by exposing it to an electric field; and

(c) causing the agent to be released from the loaded and sensitised red blood cell by applying ultrasound at a frequency and energy sufficient to cause disruption of the loaded and sensitized red blood cell but insufficient to cause disruption of unsensitised red blood cells.

9. (cancelled)

10. (canceled)

11. (previously amended) The method according to claim 8, in which the electric field is applied as an electric pulse from about 0.1 kVolts/cm to about 10 kVolts/cm under *in vitro* conditions.

12. (currently amended)The method according to claim [3 or] 11, in which the electric pulse is applied for between 1 μs and 100 milliseconds.

13. (currently amended)The method according to claim [1 or] 8, in which the ultrasound is selected from the group consisting of diagnostic ultrasound, therapeutic ultrasound and a combination of diagnostic and therapeutic ultrasound.

14. (currently amended) The method according to claim 13, in which the ultrasound is applied by an ultrasound energy source [is] at a power level of from about 0.05 W/cm^2 to about 100 W/cm^2.

15. (currently amended)A method for delivering an agent to a target site in a vertebrate, comprising the steps of:

(a) loading the red blood cell with [an] the agent *in vitro* or *ex-vivo*;

(b) sensitising *in vitro* or *ex-vivo* the red blood cell by exposing it to an electric field;

(c) introducing the loaded and sensitized red blood cell to the target site in a vertebrate by transfusion or infusion; and

(d) causing the agent to be released from the loaded and sensitised red blood cell by applying ultrasound at a frequency and energy sufficient to cause disruption of the

loaded and sensitised red blood cell but insufficient to cause disruption of unsensitised red blood cells.

16. (original) The method according to claim 15, in which the red blood cell of step (c) comprises polyethylene glycol on its surface.

17. (original) The method according to clam 15, in which the vertebrate is a mammal.

18. (original) The method according to claim 8 or 15, in which the loading of the agent is simultaneous with the sensitisation of the red blood cell.

19. (previously presented) The method according to claim 8 or 15, in which the sensitisation of the red blood cell precedes the loading of the agent.

20. (previously presented) The method according to claim 8 or 15, in which the loading of the agent precedes the sensitisation of the red blood cell.

21. (currently amended) The method according to claim [1,] 8 or 15, in which the loading is performed by a procedure selected from a group consisting of electroporation, sonoporation, microinjection, membrane intercalation, microparticle bombardment, lipid-mediated transfection, osmosis, osmotic pulsing, diffusion, endocytosis, and crosslinking to a red blood cell surface component.

22. (currently amended) The method according to claim [1,] 8 or 15, in which the agent is a polypeptide, a nucleic acid, or a virus.

23. (original) The method according to claim 22, in which the agent is combined with an imaging agent.

REASONS FOR ALLOWANCE

The following is an examiner's statement of reasons for allowance:

The provisional double patenting rejection set forth in the previous Office Action over copending application 09/748,789 is withdrawn because the claims in

the instant Application are in condition for allowance, whereas prosecution continues in the '789 application. See MPEP 804(B).

> The "provisional" double patenting rejection should continue to be made by the examiner in each application as long as there are conflicting claims in more than one application unless that "provisional" double patenting rejection is the only rejection remaining in one of the applications. If the "provisional" double patenting rejection in one application is the only rejection remaining in that application, the examiner should then withdraw that rejection and permit the application to issue as a patent, thereby converting the "provisional" double patenting rejection in the other application(s) into a double patenting rejection at the time the one application issues as a patent.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:20 AM and 3:50 PM. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, John Leguyader, be reached at 571-272-0760. The official central fax number is 703-872-9306. Inquiries of a general nature or relating to the status of the application should be directed to the Patent Analyst Trina Turner whose telephone number is 571-272-0564.

Richard Schnizer, Ph.D.

DAVE T. NGUYEN
PRIMARY EXAMINER